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<h1>TRANSMITTAL FORM</h1> <p>(to be used for all correspondence after initial filing)</p>	Application Number	10/762,652
	Filing Date	22 Jan 04
	First Named Inventor	Pravin PATE
	Group Art Unit	1626
	Examiner Name	San-Ming HUI, Esq.
	Attorney Docket Number	Triax
Total Number of Pages in This Submission		14

ENCLOSURES (check all that apply)		
<input type="checkbox"/> Fee Transmittal Form <input type="checkbox"/> Fee Attached <input type="checkbox"/> Amendment / Reply <input type="checkbox"/> After Final <input checked="" type="checkbox"/> Affidavits/declaration(s) R. Hamer <input type="checkbox"/> Extension of Time Request <input type="checkbox"/> Express Abandonment Request <input type="checkbox"/> Information Disclosure Statement <input type="checkbox"/> Certified Copy of Priority Document(s) <input type="checkbox"/> Response to Missing Parts/Incomplete Application <input type="checkbox"/> Response to Missing Parts under 37 CFR 1.52 or 1.53	<input type="checkbox"/> Assignment Papers (for an Application) <input type="checkbox"/> Drawing(s) <input type="checkbox"/> Licensing-related Papers <input type="checkbox"/> Petition <input type="checkbox"/> Petition to Convert to a Provisional Application <input type="checkbox"/> Power of Attorney, Revocation Change of Correspondence Address <input type="checkbox"/> Terminal Disclaimer <input type="checkbox"/> Request for Refund <input type="checkbox"/> CD, Number of CD(s) _____	<input type="checkbox"/> After Allowance Communication to Group <input type="checkbox"/> Appeal Communication to Board of Appeals and Interferences <input type="checkbox"/> Appeal Communication to Group (Appeal Notice, Brief, Reply Brief) <input type="checkbox"/> Proprietary Information <input type="checkbox"/> Status Letter <input type="checkbox"/> Other Enclosure(s) (please identify below):
Remarks		

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT	
Firm or Individual name	Mark Pohl, Esq., USPTO Reg. No. 35,325 Pharmaceutical Patent Attorneys, LLC 55 Madison Avenue, 4th floor, Morristown, NJ 07960-7397 USA
Signature	/s/
Date	see below date

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In The United States Patent Office

*In re Application of Pravin M.
PATEL, Stabilized Steroid
Composition And Method for
Its Preparation*

Serial No.: 10/762,652
Filing Date: 22 January 2004

DECLARATION UNDER 37 C.F.R. § 1.132

I Richard Hamer hereby make this Declaration under 37 Code of Federal
Regulations § 1.132.

1) I respectfully believe that my academic training and professional
experience qualify me as one of skill in the art of Food & Drug
Administration regulatory affairs. I attach a copy of my *curriculum vitae*
summarizing my academic training and professional experience.

2) I have read and understand the prior art of record, including Mark W.
GRINSTAFF *et al.*, *Methods for In Vivo Delivery...*, United States
Letters Patent No. 5,560,156 combined with John E. HOOVER *et al.*,
Remington's Pharmaceutical Sciences pp. 956-71 (18th ed., 1990).

3) Hydrocortisone 17-butyrate is a topical steroidal anti-inflammatory agent.

It is used topically. It is commercially available in The United States as a

In re Application of Pravin M. PATEL
Stabilized Hydrocortisone 17-Butyrate
United States Serial No. 10/762,652

topical cream, a topical lotion, a topical ointment, and a topical solution.

This is evidenced by the United States Food & Drug Administration's *Therapeutic Drug Equivalents* (Orange Book) listing for the drug product hydrocortisone 17-butyrate. (copy attached) These Food & Drug Administration records show that hydrocortisone 17-butyrate is only available as a topical drug product.

4) Hydrocortisone 17-butyrate is not currently available in the United States in any non-topical formulation. To the contrary, on information and belief formed after a reasonable inquiry, no non-topical drug product containing hydrocortisone 17-butyrate has been approved as safe and effective by The Federal Food & Drug Administration. The sale of such a non-approved drug product would constitute the sale of an unapproved new drug product. This would violate The Federal Food, Drug & Cosmetics Act, 21 U.S.C.

5) Grinstaff *at e.g.*, 26:21-31; 26:45-51, enumerates many drugs potentially suitable for inclusion in the interior fill of his synthetic blood microspheres. Grinstaff, however, fails to mention hydrocortisone 17-butyrate. This is not surprising because Grinstaff teaches an intravenous blood substitute, while hydrocortisone 17-butyrate is not recognized in the art as being acceptable for intravenous administration. Thus, an artisan of skill

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Stabilized Hydrocortisone 17-Butyrate
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in the art to which Grinstaff pertains would not consider hydrocortisone 17-butyrate suitable for inclusion in Grinstaff's micro spheres.

- 5 6) Grinstaff at 26:6-31 teaches to fill his micro spheres with cytotoxic drugs, nonsteroidal anti-inflammatory agents, steroids, and / or immunosuppressive agents.
- 7) Grinstaff teaches to dissolve these agents in a fluorocarbon, soybean oil, safflower oil, coconut oil, olive oil, cotton seed oil or other biocompatible oil.
- 10 8) Grinstaff, however, fails to teach that the fluorocarbon or bio-compatible oil must contain omega-6 acid. to the contrary, Grinstaff teaches to use several oils (e.g., fluorocarbons, coconut oil) which do not contain omega-6 acid.
- 15 9) Grinstaff also fails to mention that the fluorocarbon or bio-compatible oil must contain omega-6 acid in an amount sufficient to stabilize hydrocortisone 17-butyrate.
- 20 10) Hydrocortisone is not interchangeable with hydrocortisone 17-butyrate, which is more potent corticosteroid. For example, hydrocortisone 17-butyrate is approved only for topical administration. In contrast, hydrocortisone is approved for systemic administration as an intramuscular injection, as an enema and as an oral dosage. See Hoover

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at 965. The art of record cautions that while hydrocortisone may also be administered topically, "Systemic side effects can result from topical application." *Id.*

5 11) Similarly, hydrocortisone 17-butyrate degrades to hydrocortisone 21-butyrate. No evidence shows that hydrocortisone degrades into hydrocortisone 21-butyrate. Hydrocortisone lacks a butyrate moiety. Hydrocortisone would therefore not be expected to degrade into hydrocortisone 21-butyrate, nor into any other butyrate form.

10 12) This may be quite advantageous when administering a medical imaging agent. This would, however, render a topical medicine like hydrocortisone 17-butyrate inoperable. Adding hydrocortisone 17-butyrate to Grinstaff's micro spheres would sequester the hydrocortisone 17-butyrate, rendering it unavailable and ineffective.

15 13) Further, Grinstaff teaches that the micro spheres would sequester the hydrocortisone 17-butyrate for at least a month. Hydrocortisone 17-butyrate, however, is administered as a *skin cream*; thus, if the patient bathes at least once a month (a likely assumption for a patient who has access to prescription drugs such as hydrocortisone 17-butyrate) the patient would wash away the intact micro spheres - and their drug load -
20 before the drug is released.

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14) A patient could conceivably open the micro spheres by washing the micro sphere-treated skin with an organic solvent such as mercaptoethanol. This would be counter-productive, however, because organic solvent dries and damages skin. Compounding the problem, hydrocortisone 17-butyrate is used to treat eczema - already sensitive skin - so washing eczema-affected skin with an organic solvent would *exacerbate* the eczema, not ameliorate it.

15) In contrast to what the prior art teaches, I have found a way to stabilize hydrocortisone 17-butyrate. The instant Specification shows that after 6 months of storage at 40° C, an eczema skin cream made without added omega-6 acid has 9.17% total impurities (6.36 % hydrocortisone 21-butyrate and 2.81% other impurities). In contrast, the same skin cream with added omega-6 acid has only 5.56% total impurities (5.00 % hydrocortisone 21-butyrate and 0.56% other impurities).

16) I hereby further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment or both, under Section 1001 of Title

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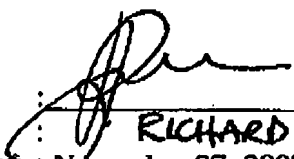
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18 of the United State Code, and that such willful false statements may jeopardize the validity of the application, any patent issuing thereon or any patent to which this verified statement is directed.

5
Signature :

Name :

Dated as of : November 27, 2007


RICHARD A. HAMER10
Attachments

Curriculum vitae.

The United States Food & Drug Administration's *Therapeutic Drug Equivalents* (Orange Book) listing for the drug product hydrocortisone 17-butyrate.

15

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Richard A. Hamer, RAC

Experience

2001-2003 Ferndale Laboratories, Inc. Ferndale, MI
Vice President, Regulatory/Clinical Affairs and QA
Responsible for staffing, training, managing and motivating regulatory affairs (4), clinical (3) and quality assurance (15) staff. Provide consultative (advisory) services as relates to implications of new product ideas, marketing approaches, and proposed manufacturing or analytical changes. Develop and implement regulatory strategies to secure approval of new and improved products in shortest possible time frame. Provide accurate interpretations and projections of future regulatory developments that may or will have a significant impact on FLI products. Establish and maintain effective working relationships with the FDA and international regulatory agencies.

1983 -2001 Richard Hamer Associates, Inc. Fort Worth, TX
Regulatory Consultant
Provide a full range of regulatory affairs consulting services to pharmaceutical and medical device manufacturers, including:

- Regulatory strategic planning.
- Preparation of investigational and marketing approval applications for new drug products and medical devices (IND, NDA, ANDA, IDE, PMA, 510(k), etc.).
- Drug Master File preparation.
- Clinical study monitoring.
- Compliance reviews of labeling and advertising.
- cGMP and QSR audits.
- FDA liaison and troubleshooting.

1982 - 1983 Alcon Laboratories, Inc. Fort Worth, TX
Consultant
Coordinated company defense efforts in U.S. vs. Alcon Laboratories (Puerto Rico), Inc. ("new drug" status law suit).

1981 - 1982 Alcon Laboratories, Inc. Fort Worth, TX
Acting Head, Regulatory Affairs
In addition to operational duties (see below), managed corporate regulatory affairs department. Coordinated with Corporate R&D, Manufacturing and Quality Assurance on regulatory issues.

1979 - 1982 Alcon Laboratories, Inc. Fort Worth, TX
Director, Regulatory Affairs - Dermatology
Managed all regulatory functions for Dermatology (Owen Laboratories) and Beauty Care (Allercreme/DuBarry/Mahdeen) Divisions, including:

- Advising Division management regarding regulatory strategies for new or improved products, proposed manufacturing or analytical changes, acquisitions and licensing agreements.
- FDA liaison.
- Review, submission, and approval monitoring of Investigational and marketing approval applications (IND, NDA, ANDA).
- Review and approval of labeling, advertising and promotional materials
- Corporate cGMP compliance audits.

1974 - 1979 Alcon Laboratories, Inc. Fort Worth, TX

Manager, Regulatory Compliance

Managed all regulatory functions for Webcon (Pediatrics/Urology products) (1974-79) and Avicon (Surgical products) (1976-79) Divisions, including:

- Advising Division management regarding regulatory strategies for new or improved products, proposed manufacturing and analytical changes, acquisitions, and regulatory implications of marketing strategies.
- FDA liaison.
- Review, submission and approval monitoring of Investigational and marketing approval applications (IND, NDA, ANDA and PMA)
- Review and approval of labeling, advertising and promotional materials.
- Corporate cGMP audits.

1973 - 1974 E.R. Squibb & Sons, Inc. Princeton, NJ

Clinical Coordinator - International Regulatory Affairs

- Evaluated clinical data for use in worldwide product registration programs.
- Prepared clinical data summaries for presentation to regulatory authorities in approximately 80 foreign countries.
- Enumerated clinical trial requirements for worldwide registration of new products and relicensing of marketed products.
- Coordinated foreign clinical trials required exclusively for product registration.
- Liaison with local subsidiaries.

1969 - 1973 E.R. Squibb & Sons, Ltd. Montreal, Canada

Coordinator - Drug Regulatory Affairs

- Evaluated CMC, preclinical and clinical data for preparation of Canadian product registration submissions.
- Liaison with HPB Canada on registration issues.
- Liaison with Squibb International Regulatory Affairs staff and consulting laboratories.
- Reviewed and approved labeling and promotional materials.

Education

1984 University of Texas at Arlington Arlington, Texas

Master of Business Administration

- Major in Economics and Marketing

1969 McGill University Montreal, Canada

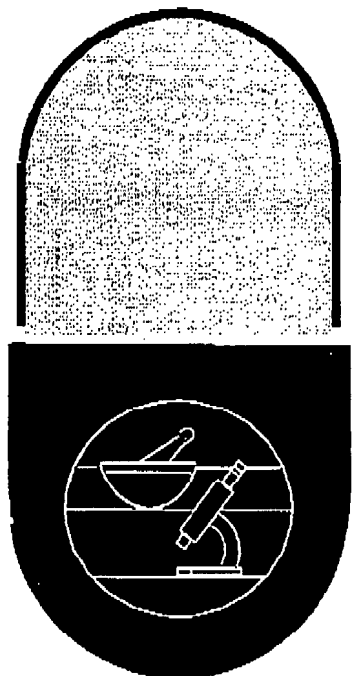
Bachelor of Science

- Chemistry/Biochemistry

Professional Memberships Regulatory Affairs Professionals Society (Regulatory Affairs Certified)
Food and Drug Law Institute

Languages Fluent in Dutch; good working knowledge of French; some German.

Computer Skills MSWord, WordPerfect, Excel



APPROVED DRUG PRODUCTS

WITH

**THERAPEUTIC
EQUIVALENCE
EVALUATIONS**

27th EDITION

**THE PRODUCTS IN THIS LIST HAVE BEEN APPROVED UNDER
SECTION 505 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT.**

**U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH
OFFICE OF PHARMACEUTICAL SCIENCE
OFFICE OF GENERIC DRUGS**

2007

APPROVED DRUG PRODUCTS with THERAPEUTIC EQUIVALENCE EVALUATIONS

The products in this list have been approved under section 505 of the Federal Food, Drug, and Cosmetic Act. This volume is current through December 31, 2006.

27th EDITION



**U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH
OFFICE OF PHARMACEUTICAL SCIENCE
OFFICE OF GENERIC DRUGS**

2007

27TH EDITION - 2007 - APPROVED DRUG PRODUCTS LIST

PRESCRIPTION DRUG PRODUCT LIST

3-199 (of 370)

HYDROCORTISONE ACETATE

POWDER; FOR RX COMPOUNDING

HYDROCORTISONE ACETATE

X GEN PHARMS

100%

N85981 001

HYDROCORTISONE ACETATE; NEOMYCIN SULFATE; POLYMYXIN B SULFATE

CREAM; TOPICAL

CORTISPORIN

+ MONARCH PHARMS

0.5%;EQ 3.5MG BASE/GM;10,000 UNITS/GM

N50218 001

Aug 09, 1985

HYDROCORTISONE ACETATE; OXYTETRACYCLINE HYDROCHLORIDE

SUSPENSION/DROPS; OPHTHALMIC

+ PFIZER

1.5%;EQ 5MG BASE/ML

N61016 001

HYDROCORTISONE ACETATE; PRAMOXINE HYDROCHLORIDE

AEROSOL, METERED; TOPICAL

EPIFOAM

BX SCHWARZ PHARMA 1%;1%

N86457 001

HYDROCORTISONE ACETATE 1% AND PRAMOXINE HYDROCHLORIDE 1%

BX BOCA PHARMA 1%;1%

N89440 001

May 17, 1988

PROCTOFOAM HC

BX SCHWARZ PHARMA 1%;1%

N86195 001

CREAM; TOPICAL

PRAMOSONE

FERNDAL LABS

0.5%;1%

N83778 001

1%;1%

N85368 001

LOTION; TOPICAL

PRAMOSONE

FERNDAL LABS

1%;1%

N85980 001

2.5%;1%

N85979 001

HYDROCORTISONE ACETATE; UREA

CREAM; TOPICAL

CARMOL HC

AT + KENWOOD LABS 1%;10%

N80505 001

U-CORT

AT TARO 1%;10%

N89472 001

Jun 13, 1988

HYDROCORTISONE BUTYRATE

CREAM; TOPICAL

HYDROCORTISONE BUTYRATE

AB TARO PHARM INDS 0.1%

N76654 001

Aug 03, 2005

LOCOID

AB + FERNDAL LABS 0.1%

N18514 001

Mar 31, 1982

LOCOID LIPOCREAM

+ FERNDAL LABS 0.1%

N20769 001

Sep 08, 1997

OINTMENT; TOPICAL

HYDROCORTISONE BUTYRATE

AB TARO 0.1%

N76842 001

Dec 27, 2004

LOCOID

AB + FERNDAL LABS 0.1%

N18652 001

Oct 29, 1982

SOLUTION; TOPICAL

HYDROCORTISONE BUTYRATE

AT TARO PHARM INDS 0.1%

N76364 001

Jan 14, 2004

LOCOID

AT + FERNDAL LABS 0.1%

N19116 001

Feb 25, 1987